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Mortality and occupational exposure to radiation: first analysis of the National Registry for Radiation Workers

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Abstract

***Objective*—To study cause specific mortality of radiation workers with particular reference to associations between fatal neoplasms and level of exposure to radiation.**

***Design*—Cohort study.**

***Setting*—United Kingdom.**

***Subjects*—95 217 radiation workers at major sites of the nuclear industry.**

***Main outcome measure*—Cause of death.**

***Results*—Most standardised mortality ratios were below 100: 83 unlagged, 85 with a 10 year lag for all causes; 84 unlagged, 86 lagged for all cancers; and 80 for all known other causes, indicating a "healthy worker effect." The deficit of lung cancer (75 unlagged, 76 lagged) was significant at the 0·1% level. Standardised mortality ratios were significantly raised (214 unlagged, 303 lagged) for thyroid cancer, but there was no evidence for any trend with external recorded radiation dose. Dose of external radiation and mortality from all cancers were weakly correlated (p=0·10), and multiple myeloma was more strongly correlated (p=0·06); for leukaemia, excluding chronic lymphatic, the trend was significant (p=0·03; all tests one tailed). The central estimates of lifetime risk derived from these data were 10·0% per Sv (90% confidence interval <0 to 24%) for all cancers and 0·76% per Sv (0·07 to 2·4%) for leukaemia (excluding chronic lymphatic leukaemia). These are, respectively, 2·5 times and 1·9 times the risk estimates recommended by the International Commission on Radiological Protection, but 90% confidence intervals are large and the commission's risk factors fall well within the range. The positive trend with dose for all cancers, from which the risk estimate was derived, was not significant. The positive association between leukaemia (except chronic lymphatic leukaemia) was significant and robust in subsidiary analyses. This study showed no association between radiation exposure and prostatic cancer.**

***Conclusion*—There is evidence for an association between radiation exposure and mortality from cancer, in particular leukaemia (excluding chronic lymphatic leukaemia) and multiple myeloma, although mortality from these diseases in the study population overall was below that in the general population. The central estimates of risk from this study lie above the most recent estimates of the International Commission on Radiological Protection for leukaemia (excluding chronic lymphatic leukaemia) and for all malignancies. However, the commission's risk estimates are well within the 90% confidence intervals from this study. Analysis of combined cohorts of radiation workers in the United States indicated lower risk estimates than the commission recommends, and when the American data are combined with our analysis the overall risks are close to those estimated by the commission. This first analysis of the National Registry for Radiation Workers does not provide sufficient evidence to justify a revision in risk estimates for radiological protection purposes.**

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Introduction

Estimates of the risks of ionising radiation rest mainly on evidence from Japanese atomic bomb survivors and from people exposed for medical reasons. These groups provide information on risks from exposure to high doses at high dose rates. There is little direct evidence of the effects of lower doses and dose rates typical of occupational exposures. To provide such direct evidence the National Radiological Protection Board, after extensive consultation with the nuclear industry and other interested groups, set up the National Registry for Radiation Workers in 1976 as the national study of radiation workers, following individuals through different employments.[1]

The first analysis of the registry covers over 95 000 radiation workers whose collective dose from external radiation is about 3200 man Sv. The essentials of the study are described in this paper; more details can be found in a separate report.[2]

Methods

Although the study population for the National Registry for Radiation Workers is broadly defined,[3] practical considerations have limited the first analysis to certain groups. Radiation workers were divided into four categories: (*a*) those in radiation work when the registry was set up; (*b*) those in employment at the inception of the study but no longer doing radiation work; (*c*) those who had left employment before the inception of the study; and (*d*) those starting radiation work after the inception of the study.

It was recognised that it would be easier to ensure that data were complete and accurate for those still in radiation work, and at the request of the participating organisations those in categories (*a*) and (*d*) were generally the first to be enrolled. The first analysis of the registry includes the following groups of workers: from British Nuclear Fuels, category (*a*) and (*d*) workers from 1 January 1976, with category (*b*) and (*c*) for Sellafield and Chapelcross; from the Ministry of Defence Atomic Weapons Establishment, workers in all categories; from the Ministry of Defence, Defence Radiological Protection Service, workers in categories (*a*) and (*d*) from 1 January 1977; from Nuclear Electric,

workers in categories (*a*) and (*d*) from 1 January 1983 at 11 sites (see table II); and from the United Kingdom Atomic Energy Authority, workers in all categories.

Certain of the participants in the registry had been included in other epidemiological studies: those of the United Kingdom Atomic Energy Authority, covering participants in employment to the end of 1979[4]; British Nuclear Fuels Sellafield, covering those in employment to the end of 1975[5]; the Atomic Weapons Establishment, covering those in employment to the end of 1982[6]; and British Nuclear Fuels Chapelcross, covering those in employment to the end of 1983.[7]

The follow up date for most workers for this first analysis of the National Registry for Radiation Workers is 31 December 1988. A combined analysis of the first three groups already studied, based on a longer period of follow up, is to be published shortly. This extension of the data on these groups will be included in a subsequent analysis of the registry. In the present analysis workers in category (c) were not followed up beyond the dates for the studies already published.

Radiation workers are given the opportunity to refuse to participate in the registry. However, less than 1·5% chose to do so, and anonymised statistical data[2] suggested that those who refused to participate were generally similar to participants.

Data collected from the employers consisted of individual identifiers, information on factors such as date of birth and sex that affect the expected pattern of mortality, and radiation dose histories. Table I gives the breakdown by date of birth and sex of participants in the registry. It shows that the study population was predominantly (92%) male and still quite young; the median date of birth was 1944.

Most of the 95 217 participants had had only one period of radiation work, but about 5% had had two or more such employments. In these cases a unified dose and employment history was set up.

For this first analysis of the registry, sites were able to provide data on exposures to external radiation only. These data are far more detailed and precise than the information normally available for occupational studies. Nevertheless, personal records of radiation exposure were kept primarily to comply with legal or administrative dose limits. For this analysis corrections were applied for notional doses, threshold doses, and changes in calibration quantity.[2] After these corrections the collective external dose was 3198 man Sv. Table II shows that 62% of the workers had a lifetime dose <10 mSv and that 9% had a lifetime dose >100 mSv. Just under half of those with doses >100 mSv worked at Sellafield, although there were also large numbers with such doses working in the United Kingdom Atomic Energy Authority, the Defence Radiological Protection Service, and Nuclear Electric.

Follow up information was obtained primarily from the National Health Service central registers for England and Wales and for Scotland. Use was also made of the tracing facilities of the records branch of the Department of Social Security and various other organisations.[2] Of the 95 217 radiation workers, 69 could not be traced satisfactorily, 1850 were recorded as having emigrated, and 6660 were recorded as having died by the end of follow up.

Personal and dose information were checked against health physics records, apart from those for the cohorts that were the subject of published reports on the Atomic Weapons Establishment, Sellafield, and United Kingdom Atomic Energy Authority workforces. A low level of errors was found. One per cent sample checks of the follow up information were

TABLE I—*Study population by year of birth and sex*

Year of birth	Men (n=87 522)	Women (n=7695)	Total (n=95 217)
Before 1915	6 141	262	6 403
1915-	3 294	163	3 457
1920-	5 978	383	6 361
1925-	6 892	410	7 302
1930-	7 378	597	7 975
1935-	7 570	718	8 288
1940-	8 236	736	8 972
1945-	10 497	583	11 080
1950-	10 120	739	10 859
1955-	11 251	1 401	12 652
1960-	7 925	1 210	9 135
1965-	2 228	492	2 720
1970-	12	1	13
Mean lifetime radiation dose (mSv)	36·0	6·1	33·6

TABLE II—*Study population by lifetime radiation dose and site of first employment*

Employer and site	Dose range (mSv) <10	10-	50-	≥100	No of workers	Collective dose (man Sv)*	Mean dose (mSv)
British Nuclear Fuels	10 223	7 464	3 083	4 847	25 617	1 805	70·4
Capenhurst	1 393	114	6	4	1 517	5	3·6
Chapelcross	462	567	351	451	1 831	141	76·7
Risley	665	56	6	4	731	3	4·5
Sellafield	5 348	4 730	2 222	4 093	16 393	1 519	92·7
Springfields	2 355	1 997	498	295	5 145	136	26·5
Ministry of Defence Atomic Weapons Establishment	8 599	1 249	239	154	10 241	85	8·3
Defence Radiological Protection Service	20 717	4 635	1 018	876	27 246	381	14·0
Navy	7 376	1 623	133	37	9 169	61	6·6
Army	2 535	315	42	49	2 941	25	8·6
RAF	4 275	491	6	1	4 773	17	3·7
Civilian	6 531	2 206	837	789	10 363	277	26·7
Nuclear Electric	4 490	2 533	696	480	8 199	198	24·1
Berkeley	127	221	111	182	641	44	68·7
Bradwell	190	245	128	85	648	28	43·3
Dungeness A	362	258	47	2	669	12	17·4
Dungeness B	541	126	17	0	684	5	8·0
Hartlepool	1 286	62	5	4	1 357	5	3·5
Heysham	496	17	2	0	515	1	1·5
Hinkley Point	498	749	214	85	1 546	49	31·4
Oldbury	332	329	49	2	712	12	17·2
Trawsfynydd	179	260	112	120	671	35	51·8
Wylfa	466	262	11	0	739	7	10·0
Not in power stations	13	4	0	0	17	0	5·6
United Kingdom Atomic Energy Authority	14 916	5 455	1 631	1 912	23 914	730	30·5
Dounreay	3 086	1 853	584	710	6 233	254	40·7
Harwell	9 300	2 701	716	730	13 447	310	23·1
Risley	598	146	20	8	772	7	9·6
Winfrith	1 932	755	311	464	3 462	159	45·9
Total	58 945	21 336	6 667	8 269	95 217	3 198	33·6

*Figures for individual sites, subtotals by employer, and total dose have been accumulated separately to greater precision than shown here, then rounded to the nearest manSv.

TABLE III—*Standardised mortality ratios (SMRs) for different causes of death*

	ICD 9th revision codes	Unlagged analysis: No of deaths Observed	Unlagged analysis: No of deaths Expected	Unlagged analysis: SMR	Lagged analysis: No of deaths Observed	Lagged analysis: No of deaths Expected	Lagged analysis: SMR
All causes	000-999	6612	8009·99	83***	4884	5737·59	85***
All known causes excluding malignant neoplasms	000-139 209-799·8						
	800-999·8	4666	5838·44	80***	3454	4148·14	83***
All malignant neoplasms	140-208	1828	2171·62	84***	1363	1589·49	86***
		Specific neoplasms					
Tongue, mouth, and pharynx	141 143-148						
	149·0	20	30·52	66†	13	22·10	59*
Oesophagus	150	60	68·68	87	53	52·88	100
Stomach	151	184	203·25	91	134	147·14	91
Large intestine	153 159·0	140	136·04	103	103	101·65	101
Rectum	154·0-154·2 154·4-154·9	78	94·86	82†	58	70·77	82
Liver, gallbladder	155-156	25	30·44	82	20	22·44	89
Pancreas	157	72	92·90	78*	54	69·86	77†
Larynx	161	15	20·26	74	10	15·08	66
Trachea, bronchus, lung and pleura	162-163	632	838·47	75***	478	628·44	76***
Bone	170	6	8·57	70	3	4·40	68
Malignant melanoma	172	20	18·63	107	12	11·68	103
Other skin cancers	173	0	5·86	0**	0	4·22	0*
All skin cancers	172-173	20	24·40	82	12	15·86	76
Breast	174	19	24·59	77	11	14·30	77
Uterus	179-182	8	7·37	109	6	4·08	147
Ovary	183	9	7·30	123	6	4·18	144
Prostate	185	89	87·27	102	80	73·05	110
Testis	186	19	12·95	147	4	5·09	79
Bladder	188	61	72·36	84	47	56·26	84
Kidney	189	33	42·31	78	26	30·90	84
Central nervous system (including brain)	191-192 225						
	239·6	59	84·63	70**	36	53·34	67*
Thyroid	193	9	4·21	214*	9	2·97	303**
Ill defined and secondary cancer	195-199	111	9568	116	87	73·73	118
All lymphatic or haematopoietic cancers	200-208 238·6	133	155·74	85†	100	99·99	100
Hodgkin's disease	201	16	23·57	68	12	11·40	105
Non-Hodgkin's lymphoma	200 202·0-202·3						
	202·5-202·9	47	46·88	100	37	31·60	117
Multiple myeloma	203·0-238·6 203·2-203·9	17	24·11	71	12	18·47	65
Leukaemia	202·4, 203·1 204-208	53	61·13	87	52	57·32	91
All leukaemia (except chronic lymphatic)	202·4, 203·1 204·0 204·2-207·7						
	207·9-208·9	45	50·91	88	44	47·35	93
Benign and ill defined neoplasms	209-239	19	26·18	73	13	16·74	78
		Non-malignant diseases					
Coronary heart disease	410-414	2389	2567·18	93***	1843	1952·39	94*
Bronchitis, emphysema, chronic obstructive disease	491-492 496						
	519	226	423·57	53***	178	319·00	56***
Aortic aneurysm	441	76	87·89	86	64	71·35	90
Diseases other than malignant neoplasms related to smoking	410-414 441 491-492 496						
	519	2691	3078·56	87***	2085	2342·73	89***
Other diseases of circulatory system	390-409 415-440						
	442-459	855	1101·67	78***	662	808·97	82***
Other diseases of respiratory system	460-490 493-495						
	497-518	227	375·07	61***	189	278·18	68***
Digestive system	520-579	137	212·17	65***	105	148·20	71***
Genitourinary system	580-629	67	89·24	75*	44	59·33	74*
All accidents and violence	800-999·8	472	582·37	81***	204	261·38	78***
Unknown causes	799·9 999·9	118			67		

†0·05<p<0·1, *p<0·05, **p<0·01, ***p<0·001.

performed at the NHS central register and the Department of Social Security, and the mortality information held at the central register for those on the National Register for Radiation Workers was also checked. There was a low level of incompleteness in the follow up data, which was corrected to a large extent by intercomparisons of data held by other research groups, the NHS central register, and the Department of Social Security.

Two types of analysis are presented. The first, external, analysis is of standardised mortality ratios in which the death rates in registry participants are compared with those in the general population of England and Wales. The second, internal, analysis is a test for trend with dose in which steps are taken to allow for factors that might obscure a dose-effect relation—for example, social class.

In the external analysis the follow up data were stratified by age in five year groups (up to 85 years), calendar years from 1955 to 1988, and sex, and comparisons were made with the corresponding mortality in England and Wales, as supplied by the Office of Population Censuses and Surveys, by calculating standardised mortality ratios with the program PERSON-YEARS.[8] Where necessary, bridge codes were used to convert death rates to disease groupings based on the ninth revision of the International Classification of Diseases. Significance tests for the standardised mortality ratios were two tailed in view of a likely "healthy worker effect."[9] Mortality rates specific to

social classes I and III[10-12] were used in an analysis of non-industrial and industrial workers respectively (this is a division, widely used in the nuclear industry, that separates social classes I, II, III non-manual from III manual, IV, V; for the armed forces the division chosen was officers *v* other ranks). To allow for the latency of any radiation effect, as well as the healthy worker effect, "lagged" analyses were also performed, in which deaths in the first two years after the start of radiation work were excluded for leukaemia and the first 10 years were excluded for other causes. The external analysis was based on the underlying cause of death recorded on the death certificate to facilitate comparison with national mortality rates.

In the internal analysis tests for trend in mortality with recorded dose from external radiation were made by using the program ARFAR,[13,14] with stratification by age (in five year groups up to 85 years), calendar period (1955-, 1960-, up to 1980-, 1985-8), sex, industrial classification, and first employer (British Nuclear Fuels Sellafield, Chapelcross, other; Nuclear Electric; Atomic Weapons Establishment; Defence Radiological Protection Service; United Kingdom Atomic Energy Authority Dounreay, Winfrith, Risley or Culcheth, Harwell or Culham or London). To allow for latency, doses were lagged by 10 years (except for leukaemia, for which a lag of two years was used); in addition, the same number of years after the start of radiation work were excluded. A score statistic was used to test for any trend in risk with dose,[13,15] and maximum likelihood estimates and 90% confidence intervals for excess relative risk per unit dose were calculated.[15] Preference was given to one tailed tests in view of the prior hypothesis that cancer rates would increase with increasing dose and because the internal analysis took additional account of confounding factors. The cause of death in this analysis was taken to be leukaemia, non-Hodgkin's lymphoma, or multiple myeloma if these were coded anywhere on the death certificate; otherwise neoplasms were selected in preference to other diseases.

Results

Table III shows standardised mortality ratios by cause of death. For the whole period of follow up (analysis without lagging), the standardised mortality ratio for all causes was 83; that for all malignant neoplasms was 84, and the ratio for all known other causes was 80. All of these ratios were significantly below 100 ($p<0·001$). For most specific types of cancer the ratios were in the range 60-100. The deficit for lung cancer (75) was significant at the 0·1% level. For all leukaemias the ratio was 87; excluding chronic lymphatic leukaemia changed this value to 88. The standardised mortality ratio for thyroid cancer was significantly greater than 100 (214, $p<0·05$), based on nine deaths.

For the lagged analysis excluding the first two years (leukaemia) or first 10 years (other cancers) after the start of radiation work, the results were broadly similar to those of the unlagged analysis (table III). The standardised mortality ratio for all malignant neoplasms was 86 ($p<0·001$) and that for leukaemia excluding chronic lymphatic leukaemia was 93. As in the unlagged analysis, the ratio for thyroid cancer was significantly higher in the lagged analysis (303, $p<0·01$).

Table IV shows that the standardised mortality ratio for all causes was low in the first few years after starting radiation work and then rose towards a plateau after 15-20 years. For all malignant neoplasms the ratio was 70 or just below 70 in the first five years but was fairly constant thereafter.

Based on mortality in the population of England and Wales, the all cause standardised mortality ratio among industrial workers was significantly greater than that for non-industrial workers (93 *v* 63; $\chi^2=201$, $p<0·001$) (table V). The ratios based on death rates specific to social class were, however, similar for industrial and non-industrial workers. These calculations were approximate because of the choice of reference population, but they served to indicate that the difference in standardised mortality ratios between industrial and non-industrial groups is a reflection of national differences rather than a special feature of this population. Standardised mortality ratios for men and women did not differ significantly (83 *v* 76, $\chi^2=1·3$, $p>0·1$) (table VI).

Table VII summarises the internal analysis. For all malignant neoplasms the trend with dose was positive, but it did not reach significance ($p=0·1$). The estimate of the excess relative risk per unit dose was 0·47/Sv (90% confidence interval −0·12 to 1·20). Out of 25 distinct specific cancer types, the estimate of trend was positive in 12 and negative in 13. For all leukaemias the trend with dose was positive and reached significance when chronic lymphatic leukaemia was excluded ($p=0·03$, one tailed test), in which case the estimated excess relative risk was 4·3/Sv (0·40 to 13·6). The increasing trend for multiple myeloma was almost significant ($p=0·06$; excess relative risk=6·9/Sv (−0·03 to 46)). One other disease grouping, ill defined and secondary tumours, had a significant ($p<0·05$) increasing trend with dose.

Several subsidiary analyses were performed. These investigated the effects of, for example, removing corrections made to the dose histories, altering the entry date for certain subgroups, excluding workers monitored for internal emitters, or excluding contributory causes of death from the internal analysis.[2] These subsidiary analyses did not suggest that the results of the main analysis were in any way atypical and, although they should not be over interpreted, the

TABLE IV—*Standardised mortality ratios (SMRs) for all causes and all cancers tabulated by year since first exposure*

No of years since first exposure	All causes of death			All cancers		
	No observed	No expected	SMR	No observed	No expected	SMR
0-1	212	314·9	87***	51	76·6	67**
2-4	450	626·8	72***	112	159·4	70***
5-9	1066	1330·7	80***	308	355·7	87*
10-14	1178	1472·6	80***	330	397·5	83***
15-19	1332	1523·9	87***	346	414·8	83***
20-29	1941	2248·2	86***	556	641·1	87***
≥30	433	492·9	88**	144	152·8	94
χ^2 for trend		20·6***			4·88*	

*p<0·05, **p<0·01, ***p<0·001.

TABLE V—*Standardised mortality ratios (SMRs) for all causes tabulated by industrial category and adjusted or not adjusted for social class*

Industrial category	No of deaths: Observed	Expected: Not adjusted	Expected: Adjusted	SMR: Not adjusted	SMR: Adjusted
Industrial	4750	5106·07	5310·00	93***	89***
Non industrial	1724	2753·63	2014·98	63***	86***
Unclassified	138	150·29		92	

***p<0·001.

TABLE VI—*Standardised mortality ratios (SMRs) for all causes tabulated by sex*

	No of deaths: Observed	Expected	SMR
Men	6434	7775·30	83***
Women	178	234·68	76***

***p<0·001.

association between death due to leukaemia and radiation was usually stronger than in the main analysis; for all cancers the results were variable.

Discussion

This analysis of the National Registry for Radiation Workers is the first in a series. For practical reasons it does not include all cohorts of radiation workers for whom dose records are held in the registry, all the most recent data from three major cohorts, nor estimates of doses from internal emitters. Nevertheless, important results have been obtained from both external and internal analyses in the present study. There is strong evidence of a healthy worker effect. Mortality is lower in radiation workers than in the general population of England and Wales—overall and for most specific causes, including cancers. There are fewer deaths from lung cancer and other cancers related to smoking and from other diseases related to smoking. Four cancer groups had significantly low standardised mortality ratios, including the grouping of cancers of trachea, bronchus, lung and pleura.

For only one cancer was the standardised mortality ratio significantly raised—thyroid cancer. As about 30 specific cancer groupings were considered it is possible that one or two positive (and negative) associations would arise by chance. This may well be the case with thyroid cancer as there was no detectable trend with external recorded dose and no evidence of common occupational exposure at any particular site; also, none of the four thyroid neoplasms for which the results of histopathology were available was of the follicular type associated with radiation.

Greatest prior interest lay in leukaemia and myelomatosis, which were associated with the highest relative risks in the data on Japanese survivors[16] and have been shown to have a high incidence in other studies of groups exposed to high radiation doses.[17] Although the standardised mortality ratios for these disease groupings were below 100, there was some evidence for an increase in mortality with radiation dose, and the association was significant for leukaemia (except chronic lymphatic leukaemia). There was no evidence for an association between prostatic cancer and radiation, in contrast to suggestions from other studies,[4,6] despite the fact that the National Registry for Radiation Workers includes the data on which the other studies were based.

One of the objectives of studies of radiation workers is to obtain direct estimates of risks from exposures to low doses of radiation at low dose rates, for comparison with the risk factors derived by the International Commission on Radiological Protection mainly from high dose and high dose rate exposures of the Japanese atomic bomb survivors, with application of a dose and dose rate effectiveness factor of 2.[18] With excess relative risks derived from internal analysis of the registry the central estimate of the total risk of radiation induced cancer for a British worker population is 10·0%/Sv, and that for leukaemia (excluding chronic lymphatic leukaemia) is 0·76%/Sv. These are, respectively, 2·5 times and 1·9 times the current values recommended by the commission for a notional (world) worker population (4%/Sv for all malignancies and 0·4%/Sv for leukaemias). Several points must be taken into account in interpreting these observations. Firstly, the greater dose range and longer follow up of the Japanese atomic bomb survivors give that study greater statistical power than the National Registry for Radiation Workers. The 90% confidence intervals from the registry are wider than those of the comparable risk estimates from the International Commission on Radiological Protection based on the Japanese data (table VIII). Furthermore, the commission's risk estimates fall well within the 90% confidence bounds from the registry. Secondly, in a combined analysis of data on about 36 000 radiation workers with a collective dose of 1140 man Sv in the United States, the central estimate of the trend in risk with dose was negative both for all malignant neoplasms and for leukaemia (excluding chronic lymphatic leukaemia) (table VIII).[19] For all malignant neoplasms, the upper limit of the 90% confidence interval in the American study was close to the central estimate from the National Registry for Radiation Workers and similar to the central estimate from the Japanese atomic bomb survivors,[16] corresponding to a lifetime risk of about 8·2%/Sv. For leukaemia, the upper limit of the 90% confidence interval in the American study was less than the central

TABLE VII—*Test for trend in mortality with dose by broad cause, specific neoplasms, and non-malignant disease*

	Dose (mSv)														Total deaths in informative strata	Score statistic	p Values		Excess relative risk (per Sv)	90% Confidence interval
	<10		10-		20-		50-		100-		200-		≥400				1 Tailed	2 Tailed		
	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected	Observed	Expected						
Broad cause																				
All causes	2030	2090·09	532	502·22	750	755·96	573	557·15	443	442·73	343	310·76	153	165·08	4824	0·59	0·28	0·56	0·101	−0·171 to 0·407
All malignant neoplasms	584	627·68	161	149·80	208	221·26	194	163·37	129	129·05	113	92·05	46	51·79	1435	1·28	0·10	0·20	0·467	−0·118 to 1·198
All known causes (excluding malignant neoplasms)	1413	1433·89	358	344·08	531	522·91	377	385·80	309	307·72	228	215·37	106	112·23	3322	0·03	0·49	0·98	0·006	−0·297 to 0·355
All known non-violent causes (excluding malignant neoplasms)	1315	1340·68	344	319·98	491	489·74	354	364·11	293	291·38	220	205·23	102	107·88	3119	0·15	0·44	0·88	0·031	−0·282 to 0·394
Accidents and violence	98	93·20	14	24·09	40	33·17	23	21·69	16	16·34	8	10·15	4	4·35	203	−0·56	0·71	0·57	−0·462	−1·294 to 1·223
Specific neoplasms																				
Mouth, tongue, pharynx	7	6·22	3	1·34	2	1·89	0	1·41	0	1·35	2	1·13	0	0·66	14	−0·92	0·81	0·38	<−1·958	<−1·958 to 2·475
Oesophagus	22	19·35	4	5·88	12	8·73	5	7·32	4	6·16	6	4·38	1	2·18	54	−0·76	0·77	0·47	−0·942	−1·778 to 1·630
Stomach	57	60·44	18	15·08	19	21·82	24	16·62	8	12·63	9	7·91	4	4·51	139	−0·13	0·55	0·90	−0·126	−1·201 to 2·133
Large intestine	49	47·33	12	12·40	13	17·92	13	13·42	17	10·08	5	7·41	4	4·44	113	−0·11	0·52	0·96	−0·121	−1·252 to 2·590
Rectum	23	26·40	7	5·95	12	9·25	6	7·62	7	6·86	5	5·91	5	3·01	65	0·96	0·17	0·34	1·278	−0·567 to 5·849
Liver, gallbladder	12	11·89	3	2·07	3	2·72	0	1·68	1	1·09	1	0·44	0	0·10	20	−0·05	0·45	0·89	−0·196	<−1·958 to 12·83
Pancreas	25	23·49	8	6·17	4	8·60	8	6·07	4	4·76	4	3·65	2	2·26	55	−0·18	0·55	0·91	−0·249	−1·467 to 3·241
Larynx	4	5·17	2	1·16	3	1·85	1	1·32	1	0·85	0	0·31	0	0·33	11	−0·81	0·76	0·48	<−1·958	<−1·958 to 36·48
Trachea, bronchus, lung, pleura	200	213·43	44	49·74	71	75·26	76	55·53	43	44·50	45	33·26	12	19·28	491	0·18	0·43	0·85	0·124	−0·798 to 1·520
Bone	2	1·64	0	0·23	1	0·30	0	0·19	0	0·17	0	0·27	0	0·20	3	−1·03	0·89	0·19	<−1·958	<−1·958 to 4·325
All skin	3	4·18	1	1·42	4	2·66	3	2·16	1	1·40	0	0·86	1	0·32	13	0·52	0·29	0·57	1·500	−1·200 to 47·82
Breast	4	5·49	3	0·77	0	1·12	1	0·38	0	0·17	0	0·07	0	0·00	8	−0·03	0·40	0·79	−0·926	<−1·958 to 155·7
Uterus	3	3·35	0	0·15	1	0·39	0	0·11	0	0·01	0	0·00	0	0·00	4	0·29	0·45	0·45	25·30	<−1·958 to 477·3
Ovary	2	3·41	0	0·32	2	0·15	0	0·09	0	0·02	0	0·00	0	0·00	4	1·23	0·12	0·12	207·1	<−1·958 to 608·2
Prostate	38	46·33	12	8·96	12	13·56	12	9·49	12	7·60	6	4·85	2	3·20	94	0·55	0·28	0·55	1·518	−1·409 to 10·68
Testis	1	2·15	2	0·64	0	1·04	2	0·76	1	0·73	0	0·51	0	0·17	6	−0·49	0·63	0·72	<−1·958	<−1·958 to 83·53
Bladder	20	24·19	5	5·76	11	7·34	4	5·56	5	4·76	5	3·65	3	1·74	53	1·56	0·07	0·14	3·575	−0·114 to 13·92
Kidney	13	13·87	2	2·73	5	3·99	4	2·58	2	2·25	1	1·21	0	0·36	27	−0·42	0·63	0·74	−1·797	<−1·958 to 11·25
Central nervous system	10	12·30	5	4·03	4	6·87	8	5·63	4	3·60	4	2·41	1	1·17	36	0·84	0·19	0·37	2·723	−1·275 to 15·08
Thyroid	4	3·31	1	0·68	1	1·82	2	1·56	0	0·84	0	0·51	1	0·28	9	0·50	0·30	0·59	1·049	−1·122 to 12·25
Ill defined and secondary neoplasms	36	43·26	11	9·25	10	13·56	11	9·51	10	7·32	8	5·14	5	2·96	91	2·69	0·01	0·02	7·282	1·825 to 17·94
Lymphatic or haematopoietic	42	44·08	14	12·91	19	17·77	13	12·69	6	10·39	11	7·33	4	3·84	109	0·55	0·30	0·61	0·607	−0·865 to 3·432
Hodgkin's disease	6	5·92	2	1·64	4	2·21	1	1·43	0	1·01	0	0·56	0	0·22	13	−1·38	0·95	0·11	<−1·958	<−1·958 to 1·190
Non-Hodgkin's lymphoma	15	14·59	7	4·53	7	6·24	1	4·71	3	4·14	5	2·63	0	1·16	38	−0·57	0·69	0·61	−1·211	<−1·958 to 3·004
Multiple myeloma	5	5·41	0	1·51	2	2·02	3	1·26	0	1·04	1	1·13	2	0·63	13	1·63	0·06	0·13	6·874	−0·029 to 45·79
Leukaemia	24	25·25	6	6·87	8	9·00	6	6·27	7	5·38	4	3·76	4	2·46	59	1·34	0·10	0·20	2·286	−0·322 to 8·367
Leukaemia (excluding chronic lymphatic)	20	21·45	4	5·34	7	6·57	3	4·56	5	4·13	4	2·92	4	2·03	47	1·95	0·03	0·07	4·277	0·396 to 13·58
Non-malignant disease																				
Smoking related	825	843·52	228	210·49	326	324·95	222	244·04	201	196·06	161	136·48	63	70·46	2026	0·50	0·31	0·62	0·132	−0·276 to 0·618
Circulatory (excluding smoking related)	274	283·05	70	60·79	90	93·02	81	68·43	55	54·30	29	40·19	22	21·22	621	−0·69	0·75	0·49	−0·279	−0·799 to 0·466
Respiratory (excluding smoking related)	82	86·71	20	16·42	27	25·18	12	17·95	14	13·76	15	9·93	5	5·06	175	0·90	0·18	0·37	0·946	−0·582 to 3·569
Digestive	38	35·71	9	10·78	18	17·24	14	12·61	6	9·65	7	5·95	3	3·06	95	−0·18	0·56	0·89	−0·184	−1·270 to 2·182
Genitourinary	17	17·29	3	4·07	6	6·05	6	4·24	5	4·06	2	3·25	2	2·05	41	−0·19	0·55	0·89	−0·279	−1·488 to 4·520
Unknown causes	33	28·52	13	8·34	11	11·80	2	7·98	5	5·96	2	3·34	1	1·06	67	−1·43	0·93	0·13	−1·241	−1·729 to 0·281

TABLE VIII—*Comparison of risk estimates from studies of Japanese atomic bomb survivors, National Registry for Radiation Workers, and combined cohort of nuclear workers in United States*

	Atomic bomb survivors[16]		National Registry for Radiation Workers	American workers*
	Whole cohort	Doses ≤500 mSv		
Cohort size	75 991		95 217	35 933
Person years	2 185 000		1 218 000	705 000
Collective dose (man Sv)	18 000		3 198	1 140
Range of doses	0-4 or more	0-0·5	0-0·5 or more	0-0·5 or more
Excess relative risk per Sv (90% confidence interval):				
All malignant neoplasms	0·41† (0·32 to 0·52)	0·38‡	0·47 (−0·12 to 1·20)	−0·99 (<−1·6 to 0·38)
Leukaemia	5·2‡ (3·8 to 7·1)	2·4‡	4·3 (0·40 to 13·6)	<−1·5 (<−1·5 to 3·4)
Lifetime risks, % per Sv (90% confidence interval):				
All malignant neoplasms	4§ (3 to 5)‖		10 (<0 to 26)	<0 (<0 to 8·2)
Leukaemia	0·4§ (0·3 to 0·55)‖		0·76 (0·07 to 2·4)	<0 (<0 to 0·60)

*Workers at Hanford, Oak Ridge and Rocky Flats.[19]
†All malignant neoplasms excluding leukaemia, based on all ages.
‡All ages at exposure.
§Derived by the International Commission on Radiological Protection applying dose and dose rate effectiveness factor of 2 to data on Japanese survivors.
‖Approximate values based on Japanese data.

estimate from the registry and was similar to that predicted by the Committee on the Biological Effects of Ionising Radiation from the fit of a linear quadratic dose-response model to the Japanese data[17 20]; this corresponds to a lifetime risk for a British population of 0·6%/Sv.[21] By contrast, the lower limit of the 90% confidence interval in the analysis of the registry is just above zero in the case of leukaemia and less than zero for all malignant neoplasms. Thus, although the confidence limits for the registry and the American study overlap, the American study points toward lower risks. Thirdly, the risk per unit dose derived from the registry may be subject to some uncertainty because only external dose was considered, and it has not been possible to take into account the possible effects of occupational exposures to other carcinogenic agents (both physical and chemical). However, if the 13 500 workers with a collective external recorded dose of about 700 man Sv and known to have been monitored for internal contamination are excluded from the analysis the results are not materially different.

Thus the risk estimates recommended by the International Commission on Radiological Protection, which were derived from high dose and high dose rate exposures, with a dose and dose rate effectiveness factor of 2, occupy a middle position between the risk estimates from two comprehensive studies of workers receiving low doses and low dose rates of radiation.[2 19] Given the statistical uncertainties, the results from these studies do not indicate that the commission's risk estimates are materially wrong. Nevertheless, the results from the first analysis of the National Registry for Radiation Workers provide valuable evidence, and future analysis of the registry, which will incorporate all registered cohorts and updated dose histories (including internal doses) and have a longer follow up, will provide a firmer basis for deriving risk estimates from low dose and low dose rate exposures.

From its inception the registry has been guided by an advisory committee of eminent epidemiologists. We are grateful to them for their guidance over many years, to Sir Richard Doll for advice, and to Dr Ethel Gilbert for making available some unpublished data.

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Detection of functional iron deficiency during erythropoietin treatment: a new approach

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Erythropoietin treatment may cause functional iron deficiency in patients receiving long term dialysis.[1-3] Such deficiency is currently detected by low transferrin saturation,[1-3] which has considerable limitations because saturation varies substantially even in normal, healthy subjects.[4 5] We conducted a multicentre prospective study of a new and more direct method of detecting iron deficient erythropoiesis. This entailed serial measurement of the percentage of hypochromic and microcytic red cells in the circulation with an automated blood count analyser.

Patients, methods, and results

Forty six patients were studied (17 from Cardiff Royal Infirmary; 15 from St Mary's Hospital, London; five from the Western Infirmary, Glasgow; and nine from West Wales General Hospital, Carmarthen). Twenty two were male and 24 female; 30 were receiving regular haemodialysis and 16 continuous ambulatory peritoneal dialysis. Nineteen patients were treated with intravenous erythropoietin 1200-4000 units thrice weekly and 27 with subcutaneous erythro-